AMENDMENTS TO THE SPECIFICATION:

Please amend the title as follows:

sFRP EXPRESSION ~~POTENTIATING~~ ENHANCING AGENT

On page 1, after the title, please insert the following new paragraph as follows:

This application is a National Stage Application of PCT/JP2005/006163, filed March 30, 2005.

Please amend paragraph [0006] as follows:

[0006] Non-patent Reference 1: Matsumine, A. et al., Science, 1996, Vol. 272, p.1020-1023.

Non-patent Reference 2: Willert, K. et al., Nature, 2003, Vol. 423, p.448-452.

Non-patent Reference 3: Reya, T. et al., Nature, 2003, Vol. 423, p.409-414.

Non-patent Reference 4: Kawano, Y. et al., Journal of Cell Science, 2003, Vol. 116, p.2627-2634.

Non-patent Reference 5: Jones, S.E. et al., BioEssays, 2002, Vol. 24, p.811-820.

Non-patent Reference 6: Suzuki, H. et al., Nature Genetics, 2004, Vol. 36, ~~p.320-322~~ p. 417-422 (published online on March 14, 2004).

Please amend paragraph [0049] as follows:

[0049] Since sFRP has a function of regulating the Wnt signal, the mechanism of tumor formation due to Dlg gene deficiency can be considered to include a cascade in which the reduced expression and/or function of ~~sDlg~~ Dlg inhibits the expression and/or function of sFRP resulting in an increase of the Wnt signal. Namely, Dlg can be considered to be a factor located

upstream of the Wnt signal transduction pathway regulated by sFRP, and to negatively regulate the Wnt signal by participating in the expression and/or function of sFRP. Therefore, the present inventors believe that Dlg inhibits the tumor formation due to the activation of the Wnt signal.

Please amend paragraph [0086] as follows:

[0086] Measurement of the expression of Dlg and sFRP can be carried out by measuring the transcription product of each of these genes, namely mRNA, or by measuring the translation product of the mRNA, namely protein. Any known gene detection methods can be used for measuring mRNA. Specifically, for example, Southern blotting, Northern blotting, the NASBA method (nucleic acid sequence-based amplification method), RT-PCR, plaque hybridization, colony hybridization, or the like, can be used. In addition, in situ RT-PCR, in situ hybridization, or the like, which allows cell level measurement can be used for the measurement. In such a gene detection method, it is useful for carrying out the measurement of a gene to use an oligonucleotide which consists of a partial sequence of the gene and has the property as a probe or a primer. The phrase "oligonucleotide having the property as a probe" means an oligonucleotide that is capable of specifically hybridizing only to the gene and consists of a characteristic sequence of the gene. The phrase "oligonucleotide having the property as a primer" means an oligonucleotide that is capable of specifically amplifying only a present polynucleotide, and consists of a characteristic sequence of a present polynucleotide. A probe and a primer may have a nucleotide sequence consisting of, preferably from about 5 to 50 nucleotides, more preferably from about 10 to 35 nucleotides, and further preferably from about 15 to 30 nucleotides. A labeled probe is normally used as the probe, but the unlabeled ~~prove~~ probe can also be used. Alternatively, the detection can also be carried out by measuring the specific

binding to a ligand that was labeled directly or indirectly. Various methods are known for labeling a probe and a ligand. For example, nick translation, random priming, or a method utilizing kinase treatment may be used. Labeling substances suitable for use include a radioactive isotope, biotin, a fluorescent substance, a chemiluminescent substance, an enzyme, an antibody, and the like. PCR is preferable as a gene detection method from the viewpoint of sensitivity. Any well-known PCR methods can be employed using a primer capable of specifically amplifying Dlg gene or sFRP gene. For example, RT-PCR may be employed. In addition, various modified PCR methods used in the art can be employed. In addition to detection of a gene, PCR allows quantitative measurement of a gene. Such an assay method may be exemplified by a competitive assay, such as an MSSA method (multi-channel simplex simulated annealing method), or PCR-SSCP (PCR-single strand conformation polymorphism), which is known as a mutation detection method that utilizes a change in mobility accompanying a structural change of a single-stranded DNA.

Please amend paragraph [0087] as follows:

[0087] Measurement of Dlg and sFRP can be carried out by employing a protein detection method or a protein quantitation method which is conventionally used. For example, Dlg and sFRP can be measured by carrying out immunoprecipitation using a specific antibody raised against Dlg or sFRP, and then analyzing with Western blotting or immunoblotting. Further, the detection of Dlg or sFRP in a paraffin tissue section or a frozen tissue section may be carried out by means of immuno-histochemical techniques using a specific antibody raised against Dlg or sFRP. The preferable methods of detecting Dlg or sFRP may be, for example, enzyme-linked immunosorvent assay (ELISA), radio immuno assay (RIA), immunoradiometric assay (IRMA),

and immunoenzymometric assay (IEMA), including a sandwich method using a monoclonal antibody and/or a polyclonal antibody. Alternatively, ~~radio immuno assay,~~ competitive binding assay, and the like, may be employed.

Please amend paragraph [0089] as follows:

[0089] Measurement of the function of sFRP can be carried out, for example, by measuring the binding of sFRP to Wnt or an inhibitory effect of sFRP on Wnt signal activation, since sFRP binds to Wnt and shows the inhibitory effect. The binding of sFRP to Wnt can be measured by a conventional binding assay. The inhibitory effect on ~~sWnt~~ Wnt signal activation can be determined by measuring the expression of β-catenin that increases with Wnt signal activation and then detecting inhibition of the expression. The expression of β-catenin can be measured by a method similar to the method of measuring Dlg expression.

Please amend paragraph [0096] as follows:

[0096] A compound obtained by the identification method according to the present invention, which has an effect of enhancing the expression and/or function of Dlg, may be used for an effective ingredient of an agent for enhancing the expression and/or function of Dlg, an agent for enhancing the expression and/or function of sFRP, an agent for inhibiting tumor formation, or an agent for preventing and/or treating a tumor disease. A compound obtained by the present identification method, which has an effect of enhancing the expression and/or function of sFRP, may be used for an effective ingredient of an agent for inhibiting tumor formation, or an agent for preventing and/or treating a tumor disease. A compound obtained by the present identification method, which has an effect of inhibiting tumor formation, may be used for an effective

ingredient of an agent for preventing and/or treating a tumor disease. In addition, ~~A~~ a compound obtained by the aforementioned identification method, which has an effect of inhibiting methylation of sFRP gene and/or an effect of inducing demethylation of sFRP gene, may be used for an effective ingredient of an agent for inhibiting methylation of sFRP gene and/or an agent for inducing demethylation of sFRP gene, an agent for enhancing the expression and/or function of sFRP, an agent for inhibiting tumor formation, or an agent for preventing and/or treating a tumor disease.

Please amend paragraph [0097] as follows:

[0097] A compound obtained by the identification method according to the present invention and a medicament containing the compound as an effective ingredient are useful for elucidating the association of Dlg with the mechanism of suppression of tumor formation and for preventing and treating a tumor disease. Further, use of at least one of the compounds and medicaments allows execution of a method of enhancing the expression and/or function of Dlg, a method of inhibiting methylation of sFRP gene and/or a method of inducing demethylation of sFRP gene, a method of enhancing the expression and/or function of sFRP, a method of inhibiting tumor formation, or a method of preventing and/or treating a tumor disease. For example, a method of enhancing the expression and/or function of Dlg may be conducted by administering at least one of the aforementioned compounds and medicaments to a subject, or by contacting in vitro at least one of the aforementioned compounds and medicaments with a cell originating in a subject or a cultured cell, and the like. A method of inhibiting tumor formation or a method of preventing and/or treating a tumor disease may be conducted by administering at least one of the aforementioned compounds and medicaments to a subject.